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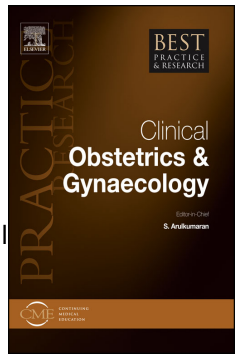

Measuring maternal, fetal and neonatal mortality: challenges and solutions

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Title: Measuring maternal, fetal and neonatal mortality: challenges and solutions

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Abstract:

Levels and causes of mortality in mothers and babies are intrinsically linked, occurring around the same time and often to the same mother-baby dyad, though mortality rates are substantially higher in babies. Measuring levels, trends and causes of maternal, neonatal and fetal mortality are important for understanding priority areas for interventions and tracking the success of interventions at the global, national, regional and local level. However, there are many measurement challenges.

This paper provides an overview of the definitions and indicators for measuring mortality in pregnant and postpartum women (maternal and pregnancy-related mortality) and their babies (fetal and neonatal mortality). We then discuss current issues in the measurement of the levels and causes of maternal, fetal and neonatal mortality, and present options for improving measurement of these outcomes. Finally, we illustrate some important uses of mortality data, including for the development of models to estimate mortality rates at the global and national level and for audits.

Key words: Stillbirth, fetal, neonatal, maternal, mortality measurement, cause-of-death measurement, indicators, data sources

Introduction

Monitoring levels of maternal mortality has been a priority on the global health agenda. Millennium Development Goal (MDG) 5 aimed to reduce the maternal mortality ratio (MMR) by 75% between 1990 and 2015. However, measuring progress over this time-period was challenging, primarily because of the scarcity of empirical data. Global tracking relied instead on modelled estimates to monitor the success.(1) These suggested that maternal mortality decreased by 44% worldwide.(2) Similar challenges were faced in tracking fetal and neonatal mortality. Neonatal deaths were not explicitly mentioned in MDG 4, which sought to reduce under-5 child mortality by two thirds, but they were increasingly recognized as comprising almost half, of child mortality globally and progressing more slowly. Neonatal mortality was estimated to have decreased by 47% worldwide.(3) Stillbirths (late fetal deaths) were excluded from the MDG targets, and consequently received less attention, although the major associated burden has been quantified more recently.(4) At the end of the MDG era, the number of deaths, albeit based on modelled estimates, remains unacceptably high: 303,000 maternal deaths(2), 2.6 million stillbirths (late fetal deaths)(5) and 2.7 million neonatal deaths.(3)

Measuring the levels and trends of maternal, neonatal, and fetal mortality is important for quantifying disease burden, understanding risk factors and determinants, identifying priority areas for interventions, programmes and policies, and evaluating the success of interventions at the global, national, regional, and local level.(6, 7) Knowing the biomedical causes of mortality in pregnant or recently-delivered women, or in their babies, is essential to direct interventions to prevent such deaths. Unfortunately, there are many challenges to measurement, but there are also numerous potential options and solutions.

This paper provides an overview of current issues and options in measuring the levels and causes of maternal, fetal, and neonatal mortality. We define the deaths and indicators, and then focus on the measurement methods, challenges and solutions, and where possible, present potential opportunities to improve measurement of maternal, neonatal and fetal death.

Definitions

To compare maternal, fetal, and neonatal mortality across populations or over time requires standardised definitions for each outcome. These were included in 10th revision of the International Classification of Diseases (ICD-10),(8) as summarised in Table 1 and described below. Various dimensions of these definitions require an ability to assess pregnancy status of women, the timing of death in relation to delivery, gestational age (or alternatively birth weight or birth length) at delivery, vital status at the start of labour and at birth and cause-of-death. The dimensions and critical time periods are shown schematically in Figure 1.

Maternal and pregnancy-related mortality

“Maternal death”, is defined in the ICD-10(8) as “the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes” (Table 1). This definition encompasses direct obstetric deaths, when death occurs because of an obstetric complication such as haemorrhage or eclampsia, and indirect obstetric deaths, when an underlying, previously-existing medical condition, or non-obstetric medical condition which developed during pregnancy, is aggravated by pregnancy. Since deaths that are accidental or incidental to the

pregnancy need to be excluded, information on cause-of-death is required to apply this definition.

However, the definition of maternal death is conceptually problematic from a measurement perspective.(9) Distinguishing indirect maternal death from incidental or accidental deaths during pregnancy or the postpartum is epidemiologically challenging, and consequently coding can be difficult. The decision whether a condition is aggravated by pregnancy or its management can either be made on a case-by-case basis, be ascribed to conditions based on epidemiologic data showing elevated incidence or case-fatality in pregnant women with the condition compared to non-pregnant women, or be decided for entire classes of conditions (e.g. deaths from external causes). Guidance is provided but is not particularly helpful; for example, ICD-MM instructs that HIV-related deaths should be classified as maternal when "there is an aggravating effect of pregnancy on HIV and the interaction between pregnancy and HIV is the underlying cause-of-death".(10) It further states that if "the woman's pregnancy status is incidental to the course of her HIV infection" then the death should not be classified as maternal. Unfortunately, ICD-MM provides no guidance on how to identify when HIV disease progression has been accelerated by pregnancy, making the coding of these deaths very difficult, particularly in the absence of detailed data. Furthermore, epidemiological studies suggest that certain causes of death that are often excluded from maternal mortality estimates, such as suicide or homicide, are more likely to occur in certain sub-sets of pregnant women compared to non-pregnant women (notably amongst younger age groups).(11)

While maternal death is the most widely used mortality definition in pregnant and postpartum women, the ICD-10 gives two further definitions that expand the deaths captured in two different ways. First, "late maternal death" lengthens the time-period, to capture maternal deaths occurring from 42 days up to one year postpartum. The 42-day postpartum cut-off has a weak evidence-base, and a few studies show women remain at elevated risk for several months after delivery.(12) Historically, a 90-day cut-off has been used,(13, 14) and some even argue that the increased mortality risk may extend beyond one year postpartum.(15) Second, "pregnancy-related death" includes any "death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause-of-death", without excluding accidental or incidental deaths in this specified time-period. This latter definition only requires information on the timing of death in relation to pregnancy (or the end of pregnancy), and not on the cause-of-death (Figure 1). As such, pregnancy-related death is comparable to neonatal and fetal deaths that are also defined primarily by time-periods, as described below.

Fetal and neonatal mortality

Livebirth is defined in ICD-10(8) as "the expulsion or extraction from its mother of a product of human conception, irrespective of the duration of the pregnancy, which, after such expulsion or extraction, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached. Heartbeats are to be distinguished from transient cardiac contractions; respirations are to be distinguished from fleeting respiratory efforts or gasps." The ICD-10(8) definition for neonatal death is the death of a live born infant in the first 28 days of life; this definition is applied nearly universally (Table 1 and Figure 1).

Fetal death is "death prior to the complete expulsion or extraction from its mother of a product of human conception, irrespective of the duration of pregnancy and which is not an induced termination of pregnancy." Death is indicated by the fetus not showing signs of being a livebirth, as described above. ICD-10 defines fetal deaths as occurring from ≥500 grams, or ≥22 weeks, or ≥25cms only. Deaths before this period are spontaneous abortions,

or miscarriages in lay terminology. Definitions and terminology for fetal deaths are applied more inconsistently -- especially amongst high-income countries with thresholds ranging from 20 weeks gestational age upwards (Figure 1).(16, 17) ICD-10 distinguishes early from late fetal deaths using birthweight, gestational age, or length criteria. ICD-10 recommends reporting both early and late fetal mortality rates, while WHO recommends using the stillbirth rate or late fetal death rate for international comparisons. The term 'stillbirth' is often used in clinical practice and common parlance to refer to any fetal death; however, it is used epidemiologically and in global estimates to refer to late fetal deaths only.

Since ICD-10 was developed several decades ago the fetal death threshold was set to be based first on birthweight criterion then gestational age and then length. However, birthweight and gestational age thresholds do not give equivalent results. For example in the USA the SBR would be 40% lower than with a 500gm threshold compared to a 22 weeks gestation threshold. Hence the threshold should be based on one parameter as it is not accurate to assume equivalence. In practice, most health facilities could measure birthweight at the time of delivery, yet in reality less than half of the world's births are weighed and fewer stillbirths are weighed. Gestational age can be difficult to assess without records from early ultrasound as the gold standard or dating based on last menstrual period.(18-20). Nevertheless, we would argue that assessment of gestational age is essential to enable correct classification of a fetal death to the early or late category to allow for international comparisons. This is used in practice in middle and high income countries, and increasingly in low income settings. It is proposed that the 11th ICD revision change to a gestational-age based fetal death threshold, in line with most high-income country reporting.

Assessing the intrapartum versus antepartum timing of fetal death is another area where definitions may be applied differently in different settings with lower level care. If evidence of a fetal heartbeat at the start of labour is not available, classification as intrapartum or antepartum often relies on an assessment of the skin of the baby (fresh versus macerated), which is not a very reliable indicator of ante or intra-partum timing of fetal death.(21, 22)

Indicators

Counting numbers of maternal, fetal, and neonatal deaths can identify countries, regions or sub-groups with the largest numeric burden, but often we are also interested in knowing where the risk of such deaths is highest. For example, due to its large population, India has a much greater number of maternal deaths compared to Sierra Leone, yet the risk of a woman in India dying of maternal causes is much lower than in Sierra Leone.(2) Identifying the risk faced by individual women or babies requires the numbers of deaths be considered in relation to a denominator at risk of these deaths. Below we describe commonly used indicators of risk, as well as others used in mortality measurement.

Maternal indicators

Assessing the risk of maternal or pregnancy-related mortality requires relating the number of such deaths in a given time-period and a given country or area, to the number of women at risk. The ideal denominator for this – the number of pregnant woman entering into the pregnancy/postpartum period, or time spent pregnant or postpartum – is difficult to obtain without conducting prospective studies of large groups of women. Instead, routine data sources are commonly used to calculate a maternal mortality ratio: the number of maternal deaths per 100,000 livebirths in a given time period: (number of deaths/livebirths) X 100,000. This livebirth denominator approximates the number of pregnancies, but excludes women who have miscarriages, induced abortions or stillbirths, while women having multiple livebirths (e.g. twins or triplets) are counted multiple times in the denominator. In some

settings, all maternity cases, including those resulting in fetal deaths, and even induced abortions, are included in the denominator.(23)

Three additional, less commonly reported, indicators are defined below:

1. Maternal (or pregnancy-related) mortality rate: deaths per 100,000 women aged 15-49 per year (mid-point population)
2. Lifetime risk of maternal (or pregnancy-related) death: the probability that a 15-year-old female will die eventually from maternal (or pregnancy-related) causes, assuming that current levels of fertility and mortality (including maternal (or pregnancy-related) mortality) do not change in the future, and taking into account competing causes of death.(24)
3. Proportion of deaths: proportion of maternal (or pregnancy-related) deaths among all deaths of women of reproductive age.

The maternal (or pregnancy-related) mortality ratio and the level of fertility influence all three indicators. For any given maternal mortality ratio, the higher the level of fertility, the higher the level of the three indicators. The lifetime risk indicator and the proportion of deaths are also influenced by death rates among non-pregnant/non-postpartum women: all else being equal, the higher the death rates in non-pregnant/non-postpartum women, the lower these two indicators will be.

Fetal and neonatal indicators

Mortality indicators for outcomes in babies are usually measured per 1,000 births. Neonatal mortality rates use livebirths as the denominator: (number of neonatal deaths)/(livebirths) X 1,000. Fetal mortality rates are: (number fetal deaths)/(livebirths + fetal deaths) X 1,000. A combined indicator for all 'perinatal deaths',(8) is used that includes all late fetal deaths (≥1,000g or ≥28 weeks) and all early neonatal deaths (days 0 – 6): (number perinatal deaths)/(livebirths + fetal deaths) X 1,000.

It is recommended that all deaths in babies less than 28 days of age, whether in-utero above a specified threshold, or in the neonatal period, are recorded by gestational age, birthweight and timing (ante- or intra-partum, and day of neonatal death). Such reporting of outcomes is of programmatic relevance. For example, the 'Intrapartum Stillbirth and Early Neonatal Death Indicator', may be used to monitor improvements of the quality of obstetric and newborn care provided at birth. It can be calculated at a facility level as: (intrapartum stillbirths + neonatal deaths within the first 24 hours of life (≥2,500g))/(livebirths+ fetal deaths (≥2,500 grams)).(25, 26)

Another, less frequently used, measure is the 'prospective fetal mortality rate': (number of fetal deaths at a gestational age per 1,000 fetal deaths at that gestational age or greater, plus livebirths). This is a more accurate denominator for those at risk, and provides an estimate of the risk of fetal death at a given gestational age.(27, 28) In high-income settings, this indicator has been used to compare the risk of fetal death with the neonatal mortality rate to determine the optimal gestational age for delivery.(29)

Current issues in measuring mortality

Despite the existence of definitions and indicators, measuring mortality can be problematic. First, deaths need to be identified, and then categorized and counted. Deaths may be misclassified because aspects of their definitions (including pregnancy/postpartum status, incidental/accidental cause-of death, gestational age, survival status at start of labour and at

delivery, and day of death postpartum) are difficult to recognize, determine, capture, or remember. They can also be misclassified because information is deliberately misreported for reasons related to blame or stigma or to protect women or avoid bureaucracy. Comparisons may be difficult because inconsistent definitions or classification systems are used, or data are not collected at all.

Sources for identifying deaths

Table 2 provides a brief overview of four main data-collection systems that can be used to identify and count maternal (or pregnancy-related), fetal, and neonatal deaths. In practice, all four have strengths, and as with most measurement systems, there are generally trade-offs between the reliability of the estimates, and practical considerations such as cost or time.

Civil registration and vital statistics (CRVS) should capture all births and deaths (including cause-of-death information assigned by a medically-qualified person) in a country, on an ongoing basis, issuing certificates for these vital events. In ICD-10, WHO recommended a checkbox on the death certificate to record a woman's pregnancy status at the time of death, enabling such systems to identify whether death was pregnancy-related.(30) Alternative systems have been used in China and India, where a "sample registration system", (sample CRVS system) is in place for a number of population clusters which have been randomly selected from a national sampling frame.(31) In theory, the national scope and the ongoing effort makes CRVS the "gold standard" for measuring all deaths. Unfortunately, CRVS systems remain weak in most areas of highest mortality burden,(32-34) missing deaths and failing to cover certain areas. Moreover, cause-of-death ascertainment, needed to define maternal deaths, is frequently poor, and substantial proportions of maternal deaths are misclassified, even in high-income settings with complete CRVS. The lack of CRVS is illustrated, for maternal mortality, in Figure 2. Fetal and early neonatal deaths, especially around viability are frequently under captured, with less than 5% globally having either a birth of death certificate.(35)

Health Management Information Systems (HMIS) are a source of data on births and deaths that occur in health facilities. They usually fail to capture births and deaths which occur at home, and in many settings also exclude events in private-sector facilities. However, HMIS can be useful for monitoring trends within facilities, particularly for fetal and early neonatal outcomes, noting the limitation that facility use, and the case-mix of woman/babies using facilities, may change over time. Further limitations occur with neonatal or maternal deaths that happen after discharge. Deaths when a women is readmitted postpartum may not be recognised as pregnancy-related, and hence missed.

Other alternatives include surveillance, through systems such as demographic surveillance sites or special studies like confidential enquiries. These may focus on deaths to women of reproductive age, and then retrospectively seek to ascertain whether the woman was pregnant or recently delivered at the time of death or may focus on deaths of pregnant or postpartum women. Alternatively, they may adopt a cohort approach and seek to identify all pregnancies and the resulting outcome for both mother and her baby. These studies tend to operate at a sub-national level as they are resource-intensive. They may also be too small to provide precise estimates of maternal mortality unless aggregated over many years.

Cross-sectional, population-based household surveys are an important source of data, particularly for neonatal mortality. A full livebirth or pregnancy history is typically used to identify births and neonatal deaths. Surveys using full pregnancy history are also potentially able to capture fetal deaths or stillbirths. Some surveys using a livebirth history have added a question regarding stillbirth, eg; the core DHS module, but for many surveys the capture of

stillbirths is implausibly low.(35, 36) Measuring maternal mortality directly via surveys by asking household members about deaths of pregnant or recently delivered women within a given time period (often in the last one or two years) requires very large sample sizes(37) or a census(38). Sisterhood method approaches ask siblings to report on the pregnancy-related deaths of their sisters, and reduces the required sample size. However, they cannot capture of information on cause-of-death or on predictors associated with increased risk because it is unreasonable to expect a sibling to know and report such details.(39)

Sources for ascertaining cause-of-death

Information on the causes of maternal, fetal and neonatal deaths are important for identifying priority interventions to reduce mortality, and is a pre-requisite for defining maternal deaths, since the definition excludes causes that are incidental to pregnancy.

Comparison of cause-of-death distributions between countries has been hampered by different classification systems, particularly for causes of stillbirths or fetal deaths.(40) To improve comparability, countries using ICD-10 should include all deaths coded to the maternal chapter (O codes) and maternal tetanus (A34) as maternal deaths, whilst all fetal and neonatal deaths should be coded to the perinatal chapter (P codes), congenital chapter (Q codes) or to a limited number of exceptions, including specific infections such as neonatal tetanus (A33) or congenital syphilis (A50).(8) In 2012, WHO published the ICD maternal mortality (ICD-MM) to be used in conjunction with the three ICD-10 volumes to reduce errors in coding maternal deaths, and to improve the attribution.(10) A similar manual to improve the coding of both stillbirths and neonatal deaths in ICD-10 is planned for release by WHO in 2016.

Ideally, detailed information on cause-of-death, distinguishing between immediate and underlying causes, should be possible to obtain from CRVS, with medical certification. Clinical diagnoses of causes can be supported with laboratory tests and even autopsies. WHO introduced a separate perinatal death certificate to obtain information on maternal and fetal conditions, but this has had limited uptake. However, population-based data on the causes of maternal, fetal and neonatal deaths are scarce in many high-burden countries, due to the lack of CRVS and medical certification.(33)

Facility records can provide information on causes of death, but the extent to which these data represent causes of these deaths at the population level is questionable given low levels of institutional delivery across many parts of Asia and sub-Saharan Africa. For example, women delivering at home and experiencing post-partum haemorrhage may die very rapidly before reaching a facility for emergency care, potentially underestimating the proportion of deaths attributable to haemorrhage if only facility level data are used.

Surveillance and surveys aiming to ascertain causes of maternal fetal and neonatal deaths in most high burden settings frequently rely on verbal autopsy (VA).(41, 42) In VA, family members or caregivers (lay reporters) of the deceased are asked about the signs and symptoms occurring before the death. Symptom data from VA interviews are then interpreted by physicians or by automated methods.(41, 43) VA has some validity for causes of neonatal death in low-resources settings, however its performance is generally worse for fetal deaths.(44-47) VA performs better at identifying overall maternal deaths when compared to identifying direct causes of maternal death.(48) Overall, however, the imprecise nature of VA, and the potential for misclassification of cause-of-death at the individual level, means results from VA are usually presented at the population level rather for individual level diagnoses.

Issues with establishing timing of death and survival status

All of these sources rely on informants, be they health professionals with access to medical records or family members, and they are therefore subject to by some important limitations. Omission or misclassification of deaths can occur for several reasons. Firstly, where the information is not known by the informant (e.g. pregnancy status in a maternal death occurring in early pregnancy or in the post-partum period or gestational age at time of fetal death). Other examples include misclassification between intrapartum fetal death and early neonatal death which is thought to be common in low-resource settings, particularly when relying on VA.
Secondly, omission or misclassification can occur where an informant deliberately withholds, or alters information. This can be motivated by desire to avoid stigma, for example families may not report pregnancy status in a young unmarried woman, termination of pregnancy, suicide or homicide. In facilities, healthcare workers may fear blame, and not report or misclassify deaths (e.g. record intrapartum stillbirths (potentially due to sub-standard care) as antepartum stillbirths (less incriminating for the birth attendant)).[11,45] Furthermore, responses to VAs can be influenced by other factors including the sex of the interviewer.(49) It has been reported that women may be unwilling to report a fetal death to a male interviewer from her village.(36)

Thirdly, accuracy and comparability can be hampered by inconsistent application of definitions, for example when fetal deaths are reported using variable definitions or for neonatal deaths where understanding the distribution of the day of death has been hampered by inconsistent use of day zero versus day one for the day of birth, and heaping of deaths on day seven (one week) affects the classification of early versus late neonatal deaths.(50)

Potential solutions to identifying deaths, and defining them accurately and consistently

We would argue that to ensure that all deaths are identified at a national level requires complete vital registration, ideally with proper medical certification of deaths, and a good classification system. ICD-11 is currently under development, along with a new single death certificate to include deaths at all ages, including stillbirths or fetal deaths. This will record women's pregnancy status and allow for the inclusion of both maternal and fetal/ neonatal contributing causes. Widespread uptake of this method of medical certification could improve our understanding of maternal, fetal and neonatal causes of death, and the links between them, and provide comparable estimates across different settings. Some settings link deaths of women to records of live-births or fetal deaths as a further way to identify possible maternal deaths.(51) Improving the classification of stillbirths and neonatal deaths and to increase comparability across settings will require a classification system with a limited number of programmatically relevant, causal categories that can be assigned using VA, but can be further expanded in settings where detailed clinical data and diagnostics are available.(52) The new ICD perinatal mortality (ICD-PM) seeks to provide such a resource to improve coding of these deaths. It has been proposed for the 11th ICD revision to change to a gestational-age based stillbirth or fetal death threshold, in line with most high-income country reporting.

For the many countries where complete vital registration is unlikely to become a reality for some years, if not decades, there are interim solutions. One solution to the challenge of capturing all maternal deaths, as is used in maternal death surveillance and response, is to first capture all deaths in women of reproductive age and then investigate the pregnancy status of the woman within 42 days of death, including with linkage to birth and fetal death records.(53) A potential solution for fetal and neonatal deaths is to investigate which survey-

based methods (e.g. birth history, pregnancy history and truncated pregnancy history) best capture these deaths. Undoubtedly, e-health can form part of the solution in a number of ways, including more timely data collection through mobile devices (m-health) and through improved HMIS systems.

Improving the ascertainment of the timing of deaths is clearly a major challenge, particularly between fetal and very early neonatal deaths, and better efforts are needed to redress drivers of misclassification. Improving gestational age assessment could include improving recall of last menstrual period, use of biomarkers, ultrasound assessment of gestational age after the first trimester and improved algorithms to enable a 'best gestational age estimate'.(18, 54) Additionally, collecting information on the fetal heart beat on admission for all facility births could improve the categorisations of a death as either in the antepartum or intrapartum period. A positive, but unintended consequence of improved training in neonatal resuscitation may be improved recording of the distinction between intrapartum fetal, and early neonatal death.(55)

Solutions are also needed to address sensitivities associated with reporting fetal, neonatal or maternal deaths. In facilities, fostering a no-blame culture of maternal and perinatal audit could have a role. Further investigation of methods to improve reporting in household surveys may focus on the interviewer, the informant, the role of stigma associated with these deaths, as well as the content of the questions.

To accurately ascertain causes of death in pregnant and postpartum women, and their babies, clearly requires more precise methods. New simplified methods for collecting cause-of-death data in resource poor settings are required, and investigations are currently underway to assess whether minimally invasive autopsies are feasible and acceptable.(56) Until other methods are available, we should strive to improve the quality of VAs and to understand the pitfalls of current methods of interpreting the data and the effects these may have on the estimated cause-specific mortality fractions. Estimates produced from VAs are likely to remain imprecise, and great caution should be applied when comparing cause-specific mortality fractions over time or in different places, given that the extent to which imprecise tools provide correct estimates will vary depending on the sensitivity, specificity and the true percentage of deaths attributable to the cause in the population.

Even with improved methods to diagnose causes of deaths, problems will still remain in how to distinguish deaths which should be classified as "maternal" (i.e. directly or indirectly related to pregnancy) from those assumed to be unrelated to the pregnancy. Recent evidence suggests it is not possible to distinguish indirect and coincidental HIV/AIDS-related deaths which calls into question the entire concept of maternal death as is currently defined.(57) Difficulties in identifying deaths aggravated by pregnancy have also been identified for other causes (e.g. malaria). We therefore agree with authors who argue that we should focus on measuring direct obstetric causes of deaths.(9) However, given that treatment provided to women within ANC/delivery services may prevent deaths which are not strictly related to the pregnancy – e.g. given that HIV-related deaths during pregnancy or the postpartum may be preventable with timely access to ART in the prenatal period – we believe it is also important, and relatively simple, to monitor all deaths to pregnant and postpartum women as well (i.e. pregnancy-related deaths). As such, we call on researchers to focus on measuring pregnancy-related mortality and, where possible, disaggregate these estimates by cause-of-death, ideally reporting cause-specific mortality ratios

Using and interpreting mortality data

Maternal, fetal and neonatal mortality data are used for numerous purposes including: examining the burden of mortality and trends in this over time; for identification of risk factors

for mortality and; for exploring effects of mortality on other outcomes (e.g. effect of a fetal death on maternal mental health, or effect of maternal death on infant survival). It can be useful to adopt a life course perspective on health problems, for example the effect of maternal health on long term outcomes for the newborn, or acute infections such as Zika virus. Mortality data can be used by a variety of end-users, from individual women and their families, to communities, front-line health providers, managers at a local or district level, national and global policy makers and researchers.

Where possible, mortality data should be available by geographical area, rural or urban, place of death, timing, underlying cause (which can include both proximal biomedical causes, and wider social determinants and factors), and other disaggregations such as socio-economic status. This can help in identifying priorities, planning and monitoring progress and advocacy purposes. For example, understanding the timing of deaths in relation to pregnancy is programmatically useful. It has been repeatedly shown that the highest risk of pregnancy-related death occurs around delivery and in the immediate postpartum period;(58) but as direct obstetric causes of deaths decline and other causes of death including non-communicable disease become more important, this pattern may shift. This has programmatic implications, increasing the importance of providing care in the antenatal and postnatal period, and requiring linkages and integration of general health services beyond just those addressing obstetric causes. However, while such disaggregations are usually possible for neonatal and fetal mortality, for maternal mortality this is more challenging as it is a relatively rare outcome. At the facility level, for example, there are only likely to be one or two maternal deaths over a year.

Cause-of-death data need to be interpreted with some caution. Changes in the percentage of deaths assigned to each cause can be driven by changes in one specific cause (see Figure 3). For example, as the percentage of deaths attributable to direct obstetric causes decrease with safe motherhood programmes we may see an increase in the proportion of deaths assigned to HIV/AIDs. This may either be due to an increase in HIV/AIDs-related deaths, or simply because the number of deaths attributable to HIV/AIDs is coming down at a slower pace than direct obstetric causes. In addition to proportions, therefore, the absolute numbers of each type of death should be related to the number at risk of dying (e.g. number of pregnant and postpartum women, number of births or the appropriate person years) to obtain absolute risks. This is particularly helpful for understanding how the risk of each cause-of-death is changing over time or between groups.

In the next sections we present two very different uses of empirical data on maternal, neonatal and fetal mortality for: 1) producing global mathematical models and 2) audit.

Estimating the mortality burden

Attempts to quantify the global burden of maternal, fetal and neonatal mortality have been hampered by a lack of data. For maternal mortality, for example, only 52% of countries have any CRVS data since 2010 (with only 40% having high-quality CRVS data), while other countries must rely on modelled estimates (Figure 2). Three main groups have developed models to estimate the levels and trends of maternal and/ or neonatal mortality, the Institute for Health Metrics and Evaluation (IHME), the Maternal Mortality Estimation Inter-agency Group (MMEIG) and the UN Interagency Group for Child Mortality Estimation (UN-IGME). To date there have not been regular attempts to quantify the global burden of fetal deaths, although WHO has led two exercises to estimate fetal deaths.(3, 59)

Whilst estimates can play an important role, especially to guide resource allocation and action in settings where high quality empirical data are not available, it is important to distinguish estimates from data and to recognize that not all estimates are equally

robust.(60) Some national estimates are derived from nationally representative data for those countries over multiple years, for example the UN-IGME estimates of overall neonatal mortality rates,(61) and therefore can be said to track mortality in each country. For other estimates, for example maternal mortality, stillbirth rate estimates and neonatal cause-of-death, the estimates for many high burden countries are not based on data from that country, but from a model bringing together data from many countries, predicting the rates and changes in rates based on country-specific covariate values. Some countries contribute little or no input data to the modelling process. The resulting estimates do not track actual changes occurring, but provide predictions of what may be occurring in countries. One example of this is seen with respect to the drop in the percentage of maternal deaths attributable to HIV/AIDS from 9.0% in 2008 to 3.8% in 2013 in the MMEIG models and from 32% in 2008 to 1.5% in 2013 in the IHME models.(62, 63) This is likely to principally reflect changes in the model assumptions. These changes to the models have been driven by not being able to accurately estimate which HIV-related deaths should be classified as indirect or coincidental to pregnancy, and will undoubtedly change as more evidence becomes available. The utility of results which are so sensitive to model assumptions is questionable, strengthening the case for focusing on improving measurement systems.(64)

Audit

Our inability to accurately measure levels and trends in mortality, as is the case in many high burden settings, contributes to the lack of an accountability mechanism in such countries, which in turn is likely to contribute to the lack of progress in reducing levels of maternal, fetal and neonatal mortality. To overcome this, audit is increasingly being used, particularly at the facility level, as a mechanism for surveillance and to identify avoidable factors leading to the death to improve quality of care. It requires a number of steps as follows:(53)

1. Establish the objectives of the audit systems
2. Identify maternal, neonatal or fetal deaths based on an appropriate case definition
3. Collect data (facilities and/or communities)
4. Investigate causes and circumstances of deaths
5. Analysis and interpret the data
6. Develop dissemination mechanism
7. Respond
8. Evaluate the audit system

Such systems have been implemented across a range of settings for investigating maternal deaths including Malawi,(65) South Africa(66) and Nigeria,(67) though not without challenges. There is evidence that audits and feedback can lead to quality improvement,(68) and positive effects have been observed on maternal health services in settings where the audit system is underpinned by a national framework with properly implemented feedback mechanisms, leadership both from committed health professionals and the ministry of health, an enabling legal framework, and a workplace culture which promotes learning.(69, 70)

Despite the link between maternal, fetal and neonatal mortality, perinatal reviews have not been as widely adopted as maternal death reviews.(70, 71) A policy review found that of the 51 “Countdown to 2015 for Maternal, Newborn and Child Health” priority countries which had a policy for maternal death notification, only 17 had a similar policy for perinatal death reviews in 2014.(70) Even in countries with a national policy on perinatal review, they are not necessarily implemented. For example, a qualitative study of maternal and perinatal death reviews in one region of Tanzania found that perinatal deaths are rarely reviewed.(72) There is, however, some limited evidence to suggest that reviewing fetal and neonatal deaths can lead to mortality reductions of round 30%, suggesting that audit could be an important tool for reducing the death of babies in high burden settings if it is effectively implemented.(73)

Conclusion

Accurate and timely measurement is important to achieve change and end preventable maternal, neonatal and fetal mortality. However, as we have illustrated in this paper there are numerous obstacles to achieving this goal, particularly in high-burden settings. These challenges range from conceptual difficulties in the definitions of maternal and fetal mortality, to challenges faced in data collection systems making it impossible to count every birth and death, to problems of intentional or unintentional misclassification and inconsistent use of definitions or use of inconsistent classification systems or indicators.

Equally there are many potential solutions, some of which we have presented in this paper. These might include expanded use of e-health platforms for data collection, and increased efforts to reduce the stigma around reporting a maternal, neonatal or fetal death. Certainly, we should consider how we can improve our definitions to enable comparable estimates, and limit the potential for misclassification. The close link between maternal, neonatal and fetal mortality – in, for example, timing and risks factors – means that many of the potential solutions will lead to improvement in measurements of all outcomes, and suggests the maternal and neonatal research communities need to collaborate to most efficiently improve measurement.

Ultimately, however, solutions to measurement issues are only likely to be properly implemented if we have the political will to do so. This has become an even more challenging task in the era of the Sustainable Development Goals, where only one of 17 goals is dedicated to health, and nested within this are sub-goals for reducing maternal and newborn mortality. In particular, it is critical that we improve visibility for tracking fetal deaths, in addition to maternal and neonatal ones.

Practice Points

Maternal, fetal and neonatal mortality data should be reported using standard definitions and, where possible, disaggregated by cause-of-death, ideally reporting cause-specific mortality ratios

These mortality data can be used for numerous purposes including: examining the burden of mortality and trends in this over time; for identification of risk factors for mortality and; for exploring effects of mortality on other outcomes

Research Agenda

The close link between maternal, neonatal and fetal mortality – in, for example, timing and risks factors – means that many of the potential solutions will lead to improvement in measurements of all outcomes, and suggests the maternal and neonatal research communities need to collaborate to most efficiently improve measurement.

References

1. Dorrington RE, Bradshaw D. Acknowledging uncertainty about maternal mortality estimates. Bulletin of the World Health Organization. Pre-pulication version.
2. Alkema L, Chou D, Hogan D, Zhang S, Moller A-B, Gemmill A, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. The Lancet. 2015.
3. UN Inter-agency Group for Child Mortality Estimation (UN-IGME). Levels and Trends in Child Mortality. http://wwwwhoint/maternal_child_adolescent/documents/levels_trends_child_mortality_2015/en/. 2015.
4. Froen JF, Friberg IK, Lawn JE, Bhutta ZA, Pattinson RC, Allanson ER, et al. Stillbirths: progress and unfinished business. Lancet. 2016.
5. Blencowe H, Cousens S, Bianchi Jassir F, Say L, Chou D, Mathers C, et al. National, regional and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analsis. Lancet Global Health 2016;4(2).
6. Gabrysch S, Zanger P, Seneviratne HR, Mbewe R, Campbell OM. Tracking progress towards safe motherhood: meeting the benchmark yet missing the goal? An appeal for better use of health-system output indicators with evidence from Zambia and Sri Lanka. Tropical Medicine & International Health. 2011;16(5):627-39.
7. Hodgins S. Achieving better maternal and newborn outcomes: coherent strategy and pragmatic, tailored implementation. Global Health: Science and Practice. 2013;1(2):146-53.
8. World Health Organization. International Classification of Diseases 10th revision (ICD-10). http://wwwwhoint/classifications/icd/ICD10Volume2_en_2010pdf?ua=1. 2010.
9. Garenne M, Kahn K, Collinson M, Gomez-Olive X, Tollman S. Protective effect of pregnancy in rural South Africa: questioning the concept of "indirect cause" of maternal death. PLoS One. 2013;8(5):e64414.
10. World Health Organization. The WHO Application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM. 2012.
11. Ronsmans C, Khlat M. Adolescence and risk of violent death during pregnancy in Matlab, Bangladesh. The Lancet. 1999;354(9188):1448.
12. Hoj L, da Silva D, Hedegaard K, Sandstrom A, Aaby P. Maternal mortality: only 42 days? BJOG : an international journal of obstetrics and gynaecology. 2003;110(11):995-1000.
13. Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. Obstetrics & Gynecology. 2010;116(6):1302-9.
14. Chen LC, Gesche MC, Ahmed S, Chowdhury A, Mosley WH. Maternal mortality in rural Bangladesh. Studies in family planning. 1974;5(11):334-41.
15. Storeng KT, Drabo S, Ganaba R, Sundby J, Calvert C, Filippi V. Mortality after near-miss obstetric complications in Burkina Faso: medical, social and health-care factors. Bull World Health Organ. 2012;90(6):418-25b.
16. Flenady V. Stillbirth: Recall to action in high-income countries. Lancet available online as part of the Ending Preventable Series. 2015.
17. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? Lancet. 2011;377(9775):1448-63.
18. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reproductive health. 2013;10 Suppl 1:S2.
19. Geerts L, Poggenpoel E, Theron G. A comparison of pregnancy dating methods commonly used in South Africa: a prospective study. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2013;103(8):552-6.
20. Lynch CD, Zhang J. The research implications of the selection of a gestational age estimation method. Paediatr Perinat Epidemiol. 2007;21 Suppl 2:86-96.

21. Gold KJ, Abdul-Mumin AR, Boggs ME, Opare-Addo HS, Lieberman RW. Assessment of "fresh" versus "macerated" as accurate markers of time since intrauterine fetal demise in low-income countries. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2014;125(3):223-7.
22. Lawn J, Shibuya K, Stein C. No cry at birth: global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths. Bull World Health Organ. 2005;83(6):409-17.
23. de Swiet M. Maternal mortality: confidential enquiries into maternal deaths in the United Kingdom. American journal of obstetrics and gynecology. 2000;182(4):760-6.
24. Wilmoth J. The lifetime risk of maternal mortality: concept and measurement. Bull World Health Organ. 2009;87(4):256-62.
25. Fauveau V. New indicator of quality of emergency obstetric and newborn care. Lancet. 2007;370(9595):1310.
26. Goldenberg RL, McClure EM, Kodkany B, Wembodinga G, Pasha O, Esamai F, et al. A multi-country study of the "intrapartum stillbirth and early neonatal death indicator" in hospitals in low-resource settings. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2013;122(3):230-3.
27. Myers SA, Waters TP, Dawson NV. Fetal, neonatal and infant death and their relationship to best gestational age for delivery at term: is 39 weeks best for everyone? Journal of perinatology : official journal of the California Perinatal Association. 2014;34(7):503-7.
28. Yudkin PL, Wood L, Redman CW. Risk of unexplained stillbirth at different gestational ages. Lancet. 1987;1(8543):1192-4.
29. Mandujano A, Waters TP, Myers SA. The risk of fetal death: current concepts of best gestational age for delivery. American journal of obstetrics and gynecology. 2013;208(3):207.e1-8.
30. MacKay AP, Rochat R, Smith JC, Berg CJ. The check box: determining pregnancy status to improve maternal mortality surveillance. American journal of preventive medicine. 2000;19(1):35-9.
31. Setel P, Sankoh O, Mathers C, Velkoff V, Rao C, Gonghuan Y, et al. Sample registration of vital events with verbal autopsy: a renewed commitment to measuring and monitoring vital statistics. Bull World Health Organ. 2005;83:611 - 7.
32. AbouZahr C, de Savigny D, Mikkelsen L, Setel PW, Lozano R, Lopez AD. Towards universal civil registration and vital statistics systems: the time is now. Lancet. 2015;386(10001):1407-18.
33. AbouZahr C, de Savigny D, Mikkelsen L, Setel PW, Lozano R, Nichols E, et al. Civil registration and vital statistics: progress in the data revolution for counting and accountability. Lancet. 2015;386(10001):1373-85.
34. Mikkelsen L, Phillips DE, AbouZahr C, Setel PW, de Savigny D, Lozano R, et al. A global assessment of civil registration and vital statistics systems: monitoring data quality and progress. Lancet. 2015;386(10001):1395-406.
35. Lawn J E, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. Lancet. 2016.
36. Haws RA, Mashasi I, Mrisho M, Schellenberg JA, Darmstadt GL, Winch PJ. "These are not good things for other people to know": how rural Tanzanian women's experiences of pregnancy loss and early neonatal death may impact survey data quality. Social science & medicine (1982). 2010;71(10):1764-72.
37. Koenig MA, Jamil K, Streatfield PK, Saha T, Al-Sabir A, Arifeen SE, et al. Maternal health and care-seeking behavior in Bangladesh: findings from a national survey. International Family Planning Perspectives. 2007:75-82.
38. Stanton C, Hobcraft J, Hill K, Kodjogbe N, Mapeta W, Munene F, et al. Every death counts: measurement of maternal mortality via a census. Bulletin of the World Health Organization. 2001;79(7):657-64.

39. Graham WJ, Ahmed S, Stanton C, Abou-Zahr C, Campbell OM. Measuring maternal mortality: an overview of opportunities and options for developing countries. BMC Med. 2008;6:12.
40. Flenady V, Wojcieszek A, Middleton P, et al. Stillbirth: Recall to action in high-income countries. Lancet in press 2016.
41. Fottrell E, Byass P. Verbal Autopsy: Methods in Transition. Epidemiologic Reviews. 2010;32(1):38-55.
42. Soleman N, Chandramohan D, Shibuya K. Verbal autopsy: current practices and challenges. Bull World Health Organ. 2006;84(3):239-45.
43. Leitao J, Desai N, Aleksandrowicz L, Byass P, Miasnikof P, Tollman S, et al. Comparison of physician-certified verbal autopsy with computer-coded verbal autopsy for cause of death assignment in hospitalized patients in low- and middle-income countries: systematic review. BMC Medicine. 2014;12:22-.
44. Aggarwal AK, Kumar P, Pandit S, Kumar R. Accuracy of WHO verbal autopsy tool in determining major causes of neonatal deaths in India. PLoS One. 2013;8(1):e54865.
45. Edmond KM, Quigley MA, Zandoh C, Danso S, Hurt C, Owusu Agyei S, et al. Diagnostic accuracy of verbal autopsies in ascertaining the causes of stillbirths and neonatal deaths in rural Ghana. Paediatric and perinatal epidemiology. 2008;22(5):417-29.
46. Nausheen S, Soofi SB, Sadiq K, Habib A, Turab A, Memon Z, et al. Validation of verbal autopsy tool for ascertaining the causes of stillbirth. PLoS One. 2013;8(10):e76933.
47. Vergnano S, Fottrell E, Osrin D, Kazembe PN, Mwansambo C, Manandhar DS, et al. Adaptation of a probabilistic method (InterVA) of verbal autopsy to improve the interpretation of cause of stillbirth and neonatal death in Malawi, Nepal, and Zimbabwe. Popul Health Metr. 2011;9:48.
48. Chandramohan D, Rodrigues LC, Maude GH, Hayes RJ. The validity of verbal autopsies for assessing the causes of institutional maternal death. Studies in Family Planning. 1998:414-22.
49. Ronsmans C, Vanneste AM, Chakraborty J, Van Ginneken J. A comparison of three verbal autopsy methods to ascertain levels and causes of maternal deaths in Matlab, Bangladesh. Int J Epidemiol. 1998;27(4):660-6.
50. Oza S, Cousens SN, Lawn JE. Estimation of daily risk of neonatal death, including the day of birth, in 186 countries in 2013: a vital-registration and modelling-based study. The Lancet Global health. 2014;2(11):e635-44.
51. Gissler M, Berg C, Bouvier-Colle MH, Buekens P. Methods for identifying pregnancy-associated deaths: population-based data from Finland 1987–2000. Paediatric and perinatal epidemiology. 2004;18(6):448-55.
52. World Health Organization. The WHO Application of ICD-10 to perinatal deaths: ICD-Perinatal Mortality (ICD-PM). http://wwwwhoint/reproductivehealth/projects/02-ICD-PMpdf?ua=1. 2015.
53. Hounton S, De Bernis L, Hussein J, Graham WJ, Danel I, Byass P, et al. Towards elimination of maternal deaths: maternal deaths surveillance and response. Reproductive health. 2013;10:1.
54. Moore KA, Simpson JA, Thomas KH, Rijken MJ, White LJ, Lu Moo Dwell S, et al. Estimating Gestational Age in Late Presenters to Antenatal Care in a Resource-Limited Setting on the Thai-Myanmar Border. PLoS One. 2015;10(6):e0131025.
55. Msemo G, Massawe A, Mmbando D, Rusibamayila N, Manji K, Kidanto HL, et al. Newborn mortality and fresh stillbirth rates in Tanzania after helping babies breathe training. Pediatrics. 2013;131(2):e353-60.
56. Bassat Q, Ordi J, Vila J, Ismail MR, Carrilho C, Lacerda M, et al. Development of a post-mortem procedure to reduce the uncertainty regarding causes of death in developing countries. The Lancet Global Health.1(3):e125-e6.
57. Calvert C, Ronsmans C. Pregnancy and HIV disease progression: a systematic review and meta-analysis. Trop Med Int Health. 2015;20(2):122-45.
58. Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why. The Lancet.368(9542):1189-200.

59. Cousens S, Blencowe H, Stanton C, Chou D, Ahmed S, Steinhardt L, et al. National, regional, and worldwide estimates of stillbirth rates in 2009 with trends since 1995: a systematic analysis. Lancet. 2011;377(9774):1319-30.
60. Oza S, Lawn JE, Hogan DR, Mathers C, Cousens SN. Neonatal cause-of-death estimates for the early and late neonatal periods for 194 countries: 2000-2013. Bull World Health Organ. 2015;93(1):19-28.
61. UN Inter-agency Group for Child Mortality Estimation (UN-IGME). Child Mortality Estimates. http://wwwchildmortalityorg/.
62. WHO, UNICEF, UNFPA, The World Bank, and the United Nations Population Division. Trends in Maternal Mortality: 1990 to 2013 http://wwwwhoint/reproductivehealth/publications/monitoring/maternal-mortality-2013/en/. 2014.
63. Kassebaum NJ, Bertozzi-Villa A, Coggeshall MS, Shackelford KA, Steiner C, Heuton KR, et al. Global, regional, and national levels and causes of maternal mortality during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9947):980-1004.
64. Graham WJ, Adjei S. A call for responsible estimation of global health. PLoS Med. 2010;7(11):e1001003.
65. Owolabi H, Ameh CA, Bar-Zeev S, Adaji S, Kachale F, van den Broek N. Establishing cause of maternal death in Malawi via facility-based review and application of the ICD-MM classification. BJOG : an international journal of obstetrics and gynaecology. 2014;121 Suppl 4:95-101.
66. National Committee for Confidential Enquiry into Maternal Deaths. Saving Mothers 2011-2013: Sixth report on the Confidential Enquiries into Maternal Deaths in South Africa.
67. Achem FF, Agboghoroma CO. Setting up facility-based maternal death reviews in Nigeria. BJOG : an international journal of obstetrics and gynaecology. 2014;121 Suppl 4:75-80.
68. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. The Cochrane database of systematic reviews. 2012;6:Cd000259.
69. Lewis G. The cultural environment behind successful maternal death and morbidity reviews. BJOG : an international journal of obstetrics and gynaecology. 2014;121 Suppl 4:24-31.
70. Kerber KJ, Mathai M, Lewis G, Flenady V, Erwich JJ, Segun T, et al. Counting every stillbirth and neonatal death through mortality audit to improve quality of care for every pregnant woman and her baby. BMC pregnancy and childbirth. 2015;15 Suppl 2:S9.
71. Amaral E, Souza JP, Surita F, Luz AG, Sousa MH, Cecatti JG, et al. A population-based surveillance study on severe acute maternal morbidity (near-miss) and adverse perinatal outcomes in Campinas, Brazil: the Vigimoma Project. BMC pregnancy and childbirth. 2011;11(1):9.
72. Armstrong CE, Lange IL, Magoma M, Ferla C, Filippi V, Ronsmans C. Strengths and weaknesses in the implementation of maternal and perinatal death reviews in Tanzania: perceptions, processes and practice. Trop Med Int Health. 2014;19(9):1087-95.
73. Pattinson R, Kerber K, Waiswa P, Day LT, Mussell F, Asiruddin SK, et al. Perinatal mortality audit: counting, accountability, and overcoming challenges in scaling up in low- and middle-income countries. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2009;107 Suppl 1:S113-21, s21-2.
74. Graham W, Brass W, Snow RW. Estimating maternal mortality: the sisterhood method. Studies in family planning. 1989:125-35.

Tables and Figures

Figures

Figure 1: Schematic representation of times when maternal, fetal and neonatal deaths occur in relation to pregnancy. Adapted from Lawn et al, 2011(17)

Figure 2: Empirically-measured data available for producing maternal mortality estimates (since 2010). Source: Produced using information from Alkema et al. 2015 & WHO, Trends in maternal mortality: 1990-2015 (available from: http://apps.who.int/iris/bitstream/10665/194254/1/9789241565141_eng.pdf?ua=1)

Figure 3: Schematic showing four categories of ICD causes of neonatal death, shown as rates (bar) and percentages (pie) for the world, and two countries. Comparing the pies for "pre-term birth" (in blue) suggests that deaths in this category are roughly the same world-wide, and in Country A and Country B. However the rates show that the preterm death rate is very low in Country A and very high in Country C.

Table 1: ICD-10 definitions of maternal, fetal and neonatal deaths(8)

Indicator	**Primary threshold:**	**Alternative threshold/ definition:**
Maternal death	A death while pregnant or within 42 days of termination of pregnancy, irrespective of the duration & the site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.	90 days (13) or 40 days(74) (13)
Late maternal death	A maternal death from direct or indirect obstetric causes, more than 42 days, but less than one year, after termination of pregnancy	
Pregnancy-related death	A death while pregnant or within 42 days of termination of pregnancy, irrespective of the cause-of-death	
Early fetal death*	A baby born with no signs of life with birthweight ≥500 - <1000gms	Gestational age ≥22 weeks or length ≥25cm (if birthweight not available)
Late fetal death	A baby born with no signs of life with birthweight ≥1000 gms	Gestational age ≥28 weeks or length ≥35cm (if birthweight not available)
Intrapartum fetal death	A fetal death occurring after the onset of labour, but before birth	A baby born with no signs of life, but no evidence of skin maceration (Fresh stillbirth) is commonly used as surrogate marker(22)
Antepartum fetal death	A fetal death occurring prior to the onset of labour	A baby born with no signs of life, with evidence of skin maceration (Macerated stillbirth) is commonly used as surrogate marker(22)
Perinatal Death	Composite indicator including all late fetal deaths and early neonatal deaths	Other composite indicators for perinatal deaths are described in the text
Early neonatal death	A death of a liveborn baby at 0-6 days of age regardless of gestational age or birthweight	
Late neonatal death	A death of a liveborn baby at 7 - 27 days of age regardless of gestational age or birthweight	
Neonatal death	A death of a liveborn baby at 0 - 27 days of age regardless of gestational age or birthweight	Deaths in the first month of life

* Non-induced pregnancy losses with a birthweight <500g (or gestational age <22 weeks or length <25cm) are defined as miscarriages in ICD-10, although many countries (e.g. USA, Australia) report fetal deaths using a lower gestational age (≥20 weeks definition)

Table 2: Mechanisms for identifying maternal, fetal and neonatal deaths

Mechanism	Active vs passive data collection	Frequency	Notes
Civil registration	Passive	Continuous	Works well with high coverage, completeness of births and deaths registration, and with good ascertainment of cause-of-death. Can be easier to implement in urban areas. Low coverage in highest burden areas (Figure 2 for maternal). Sample vital registration approaches are taken in China and India
Health Information Management Systems	Passive	Continuous	Widespread in public-sector facilities in many countries. Quality variable, and data may not filter-up to aggregated levels. Frequently, low inclusion of private-sector. Platforms include District Health Information Systems 2 (www.dhis2.org/)
Surveillance	Predominantly Active	Continuous or periodic	Surveillance can be of whole populations, of pregnancies and their outcomes, or of deaths (either all deaths of reproductive aged females, or all pregnancy-related deaths. Can occur for short or prolonged periods (e.g. demographic surveillance sites). Surveillance can range from continuous case detection, to surveillance visits up to 1 year apart.
Population-based surveys (e.g. RHS, DHS and MICS) or Census	Active	Intermittent	Surveys are the main source of mortality outcomes on the 45 million births occurring outside facilities. Fetal deaths are frequently omitted, and capture of fetal and early neonatal deaths may be of poor quality. Measuring maternal mortality based on reported household deaths via surveys requires very large sample sizes, or a census. Sisterhood method approaches reduce this requirement but limits the capture of information on cause-of-death or on co-variates (see main text for reasons).

RHS=Reproductive Health Surveys (http://ghdx.healthdata.org/series/reproductive-health-survey-rhs)
DHS=Demographic and Health Surveys (http://www.dhsprogram.com/)
MICS=Multiple Indicator Cluster Surveys (http://mics.unicef.org/)

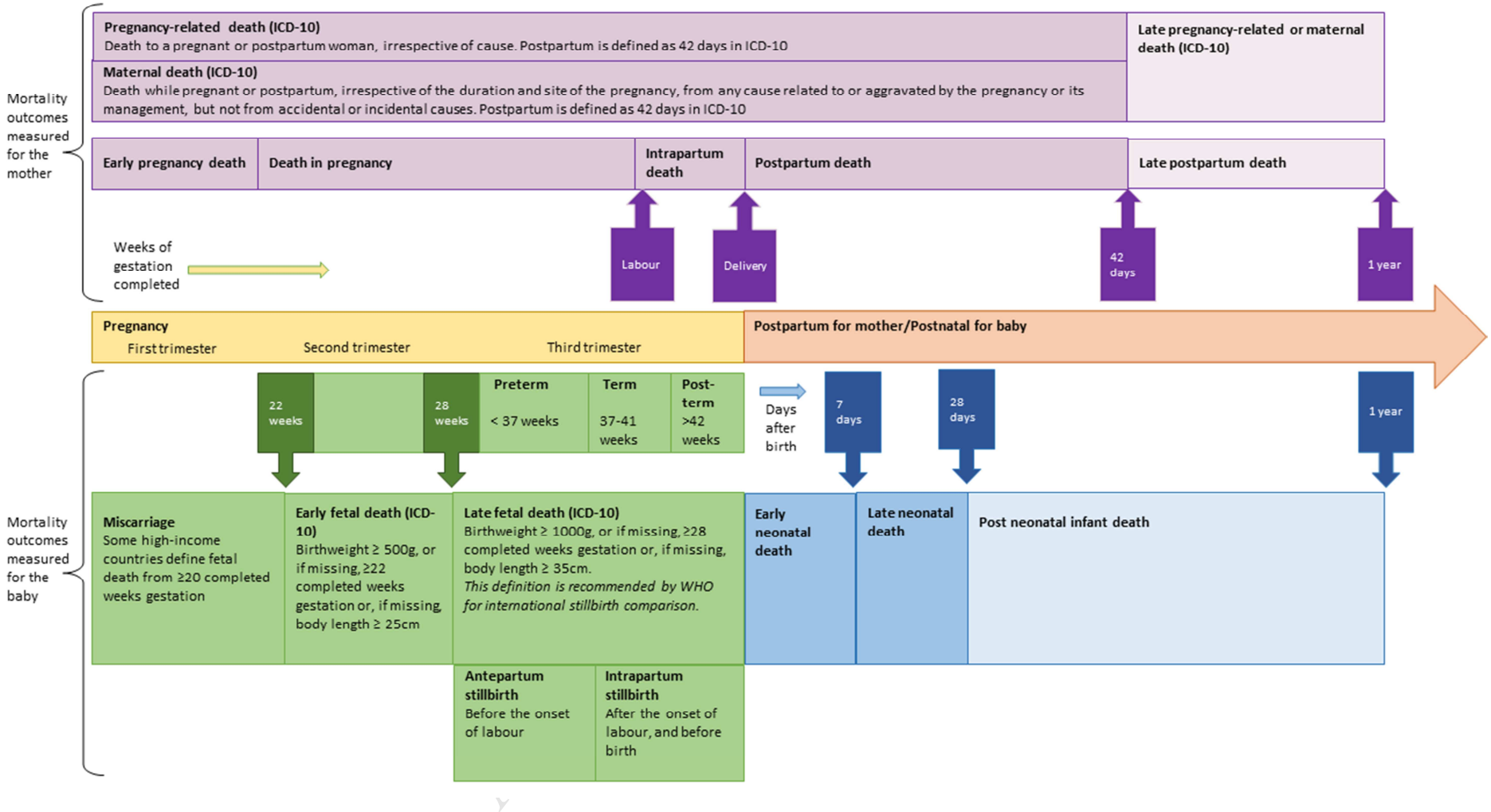
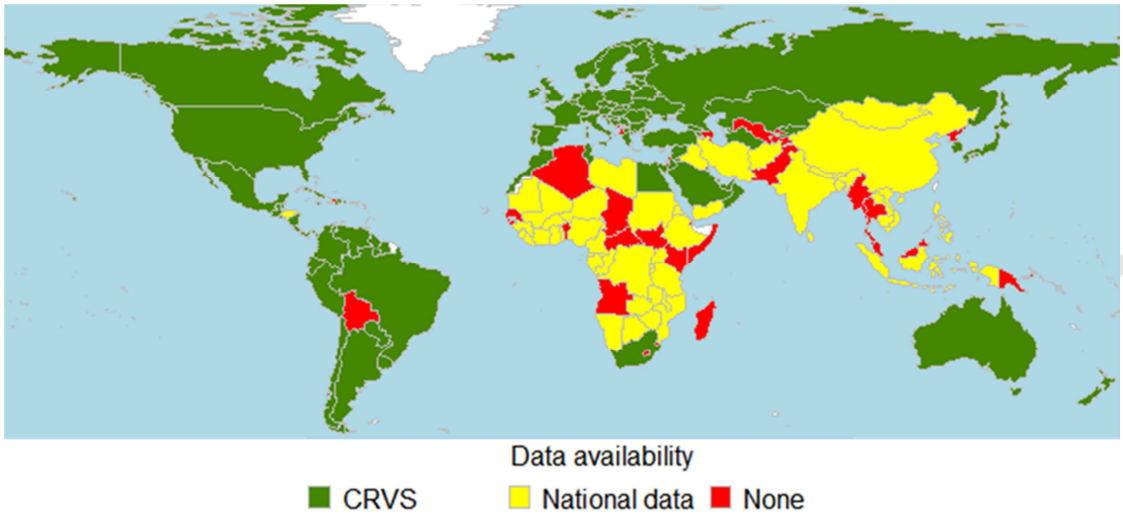


Figure 1: Schematic representation of times when maternal, fetal and neonatal deaths occur in relation to pregnancy. Adapted from Lawn et al, 2011(17)



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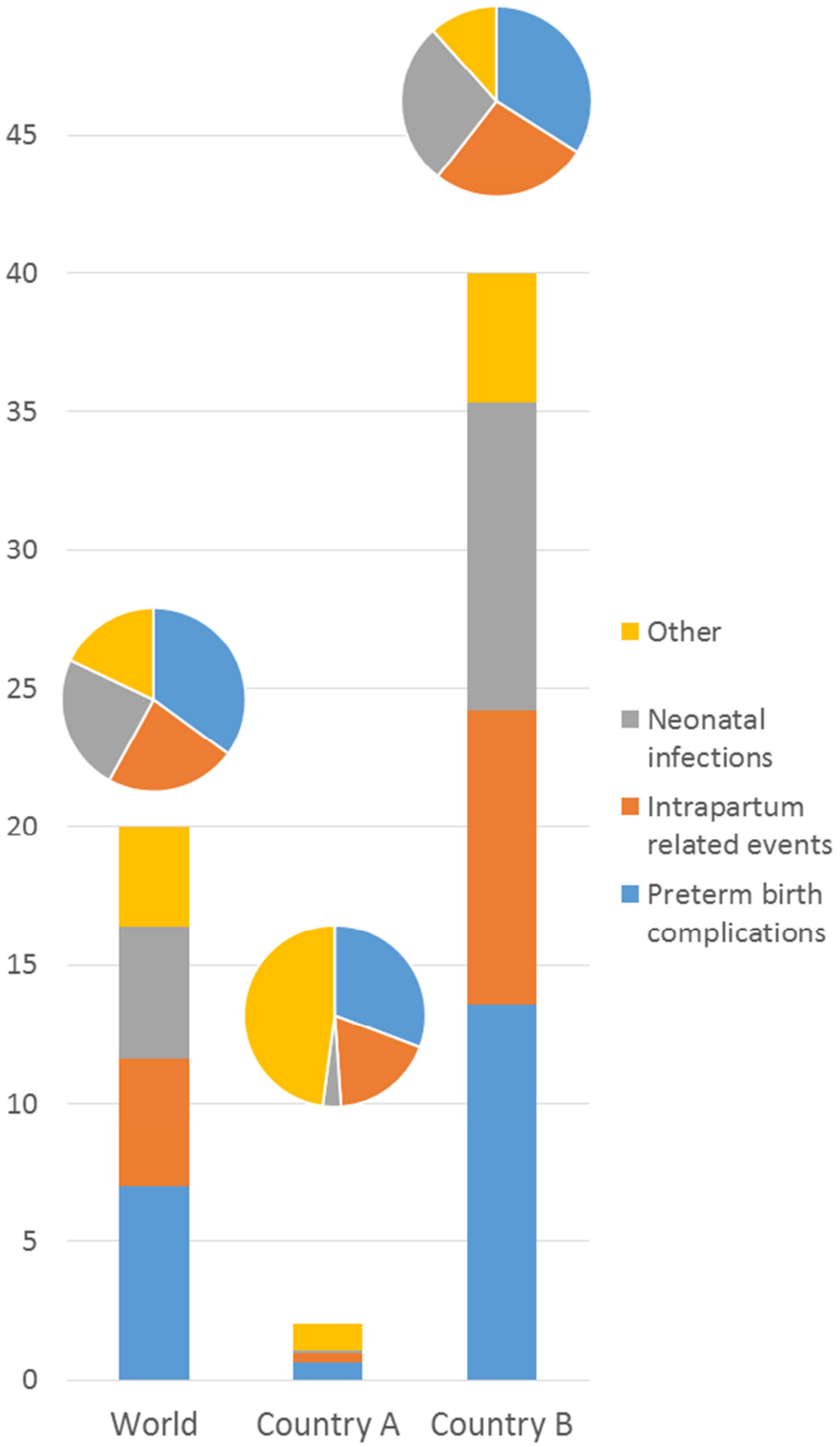
45
40
35
30
25
20
15
10
5
0
World
Country A
Country B
Other
Neonatal infections
Intrapartum related events
Preterm birth complications

1. Levels and causes of mortality in mothers and babies are intrinsically linked
2. Measuring levels, trends and causes of maternal, neonatal and fetal mortality are important for understanding priority areas for interventions and tracking their success
3. There are standard definitions and indictors of measuring mortality in pregnant and postpartum women and their babies, presented in this paper
4. Measurement challenges exist, awareness and attention to these would improve the measurement for these outcomes